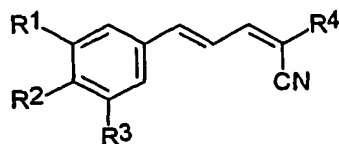


**WE CLAIM:**

1. A method of inhibiting secretion of vascular endothelial growth factor in an animal in need of such inhibition, comprising administering to the animal an effective amount of a compound of Formula I, or a salt, solvate, prodrug, or hydrate thereof:



I

wherein

$R^1$  and  $R^2$  are each independently selected from H, OH,  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy,  $NH_2$ ,  $NH-C_{1-6}$ alkyl,  $N(C_{1-6}alkyl)(C_{1-6}alkyl)$ , SH,  $S-C_{1-6}alkyl$ ,  $O-Si(C_{1-6}alkyl)(C_{1-6}alkyl)(C_{1-6}alkyl)$ ,  $NO_2$ ,  $CF_3$ ,  $OCF_3$  and halo;

$R^3$  is selected from H, OH,  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy,  $NH_2$ ,  $NH-C_{1-6}alkyl$ ,  $N(C_{1-6}alkyl)(C_{1-6}alkyl)$ , SH,  $S-C_{1-6}alkyl$ ,  $O-Si(C_{1-6}alkyl)(C_{1-6}alkyl)(C_{1-6}alkyl)$ ,  $NO_2$ , halo and  $CH_2-S-(CH_2)_n Ar$ ;

$R^4$  is selected from  $C(X)R^5$ ,  $SO_3 Ar$ ,  $NH_2$ ,  $NH-C_{1-6}alkyl$ ,  $N(C_{1-6}alkyl)(C_{1-6}alkyl)$ ,  $P(O)(OH)_2$ ,  $P(O)(OC_{1-6}alkyl)_2$ , and  $C(NH_2)=C(CN)_2$ ;

X is selected from O, S, NH and  $N-C_{1-6}alkyl$ ;

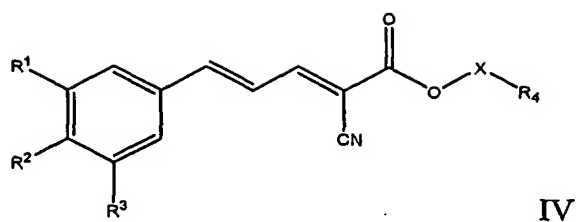
$R^5$  is selected from  $NH_2$ , OH,  $NH(CH_2)_p Ar$ ,  $NH(CH_2)_p OH$ ,  $(CH_2)_p OC_{1-6}alkyl$ ,  $C_{1-6}alkyl$ ,  $C_{1-6}alkoxy$ ,  $NHNH_2$ ,  $NHC(O)NH_2$ ,  $NHC(O)C_{1-6}alkoxy$ , N-morpholino and N-pyrrolidino; and

Ar is an aromatic or heteroaromatic group, unsubstituted or substituted with 1-4 substituents, independently selected from OH,  $C_{1-6}alkyl$ ,  $C_{1-6}alkoxy$ ,  $NH_2$ ,  $NH-C_{1-6}alkyl$ ,  $N(C_{1-6}alkyl)(C_{1-6}alkyl)$ , SH,  $S-C_{1-6}alkyl$ ,  $NO_2$ ,  $CF_3$ ,  $OCF_3$  and halo;

n is 0 to 4; and

p is 1-4.

2. A method of inhibiting secretion of vascular endothelial growth factor in an animal in need of such inhibition, comprising administering to the animal an effective amount of a compound of Formula IV, or a salt, solvate, prodrug, or hydrate thereof:



wherein

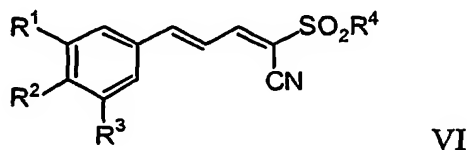
$R^1$ ,  $R^2$  and  $R^3$  are each independently selected from H, OH,  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy,  $NH_2$ ,  $NH-C_{1-6}$ alkyl,  $N(C_{1-6}$ alkyl)( $C_{1-6}$ alkyl), SH,  $S-C_{1-6}$ alkyl,  $NO_2$ ,  $CF_3$ ,  $OCF_3$  and halo;

$R^4$  is unsubstituted Ar, or Ar substituted with 1-4 substituents, independently selected from  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy and halo;

X is selected from  $(CH_2CH_2O)_n$  and  $(CH_2)_n$ , and

$n = 1-4$ .

3. A method of inhibiting secretion of vascular endothelial growth factor in an animal in need of such inhibition, comprising administering to the animal an effective amount of a compound of Formula VI, and/or a salt, solvate, prodrug, or hydrate thereof:

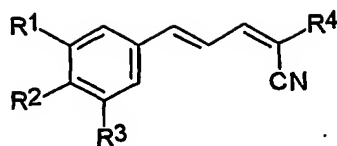


wherein

$R^1$ ,  $R^2$  and  $R^3$  are each independently selected from H, OH,  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy,  $NH_2$ ,  $NH-C_{1-6}$ alkyl,  $N(C_{1-6}$ alkyl)( $C_{1-6}$ alkyl), SH,  $S-C_{1-6}$ alkyl,  $NO_2$ ,  $CF_3$ ,  $OCF_3$  and halo; and

$R^4$  is selected from  $C_{1-6}$ alkyl, phenyl and pyridyl, wherein phenyl and pyridyl are unsubstituted or substituted with 1-4 substituents, independently selected from  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy and halo.

4. A method of inhibiting an effect of vascular endothelial growth factor in an animal in need of such inhibition, comprising administering to the animal an effective amount of a compound of Formula I, or a salt, solvate, prodrug, or hydrate thereof:



I

wherein

$R^1$  and  $R^2$  are each independently selected from H, OH,  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy,  $NH_2$ ,  $NH-C_{1-6}$ alkyl,  $N(C_{1-6}alkyl)(C_{1-6}alkyl)$ , SH,  $S-C_{1-6}alkyl$ ,  $O-Si(C_{1-6}alkyl)(C_{1-6}alkyl)(C_{1-6}alkyl)$ ,  $NO_2$ ,  $CF_3$ ,  $OCF_3$  and halo;

$R^3$  is selected from H, OH,  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy,  $NH_2$ ,  $NH-C_{1-6}alkyl$ ,  $N(C_{1-6}alkyl)(C_{1-6}alkyl)$ , SH,  $S-C_{1-6}alkyl$ ,  $O-Si(C_{1-6}alkyl)(C_{1-6}alkyl)(C_{1-6}alkyl)$ ,  $NO_2$ , halo and  $CH_2-S-(CH_2)_n Ar$ ;

$R^4$  is selected from  $C(X)R^5$ ,  $SO_3 Ar$ ,  $NH_2$ ,  $NH-C_{1-6}alkyl$ ,  $N(C_{1-6}alkyl)(C_{1-6}alkyl)$ ,  $P(O)(OH)_2$ ,  $P(O)(OC_{1-6}alkyl)_2$ , and  $C(NH_2)=C(CN)_2$ ;

X is selected from O, S, NH and  $N-C_{1-6}alkyl$ ;

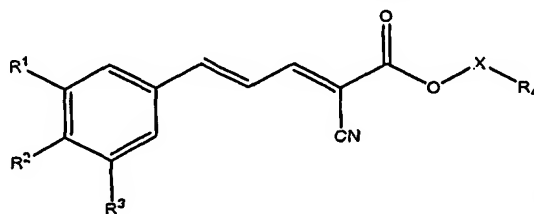
$R^5$  is selected from  $NH_2$ , OH,  $NH(CH_2)_p Ar$ ,  $NH(CH_2)_p OH$ ,  $(CH_2)_p OC_{1-6}alkyl$ ,  $C_{1-6}alkyl$ ,  $C_{1-6}alkoxy$ ,  $NHNH_2$ ,  $NHC(O)NH_2$ ,  $NHC(O)C_{1-6}alkoxy$ , N-morpholino and N-pyrrolidino; and

Ar is an aromatic or heteroaromatic group, unsubstituted or substituted with 1-4 substituents, independently selected from OH,  $C_{1-6}alkyl$ ,  $C_{1-6}alkoxy$ ,  $NH_2$ ,  $NH-C_{1-6}alkyl$ ,  $N(C_{1-6}alkyl)(C_{1-6}alkyl)$ , SH,  $S-C_{1-6}alkyl$ ,  $NO_2$ ,  $CF_3$ ,  $OCF_3$  and halo;

n is 0 to 4; and

p is 1-4.

5. A method of inhibiting an effect of vascular endothelial growth factor in an animal in need of such inhibition, comprising administering to the animal an effective amount of a compound of Formula IV, or a salt, solvate, prodrug, or hydrate thereof:



IV

wherein

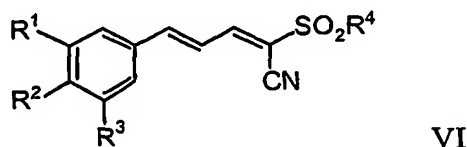
$R^1$ ,  $R^2$  and  $R^3$  are each independently selected from H, OH,  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy,  $NH_2$ ,  $NH-C_{1-6}$ alkyl,  $N(C_{1-6}$ alkyl)( $C_{1-6}$ alkyl), SH,  $S-C_{1-6}$ alkyl,  $NO_2$ ,  $CF_3$ ,  $OCF_3$  and halo;

$R^4$  is unsubstituted Ar, or Ar substituted with 1-4 substituents, independently selected from  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy and halo;

X is selected from  $(CH_2CH_2O)_n$  and  $(CH_2)_n$ , and

$n = 1-4$ .

6. A method of inhibiting an effect of vascular endothelial growth factor in an animal in need of such inhibition, comprising administering to the animal an effective amount of a compound of Formula VI, and/or a salt, solvate, prodrug, or hydrate thereof:

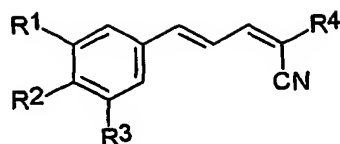


wherein

$R^1$ ,  $R^2$  and  $R^3$  are each independently selected from H, OH,  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy,  $NH_2$ ,  $NH-C_{1-6}$ alkyl,  $N(C_{1-6}$ alkyl)( $C_{1-6}$ alkyl), SH,  $S-C_{1-6}$ alkyl,  $NO_2$ ,  $CF_3$ ,  $OCF_3$  and halo; and

$R^4$  is selected from  $C_{1-6}$ alkyl, phenyl and pyridyl, wherein phenyl and pyridyl are unsubstituted or substituted with 1-4 substituents, independently selected from  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy and halo.

7. The method of claim 4, 5, or 6, wherein the effect of vascular endothelial growth factor is angiogenesis, vasculogenesis, arteriogenesis, vascular permeability or inflammation.
8. A method of treating a disorder caused or contributed to by vascular endothelial growth factor in an animal in need of such treatment, comprising administering to the animal an effective amount of a compound of Formula I, or a salt, solvate, prodrug, or hydrate thereof:



I

wherein

$R^1$  and  $R^2$  are each independently selected from H, OH,  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy,  $NH_2$ ,  $NH-C_{1-6}$ alkyl,  $N(C_{1-6}alkyl)(C_{1-6}alkyl)$ , SH,  $S-C_{1-6}alkyl$ ,  $O-Si(C_{1-6}alkyl)(C_{1-6}alkyl)(C_{1-6}alkyl)$ ,  $NO_2$ ,  $CF_3$ ,  $OCF_3$  and halo;

$R^3$  is selected from H, OH,  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy,  $NH_2$ ,  $NH-C_{1-6}alkyl$ ,  $N(C_{1-6}alkyl)(C_{1-6}alkyl)$ , SH,  $S-C_{1-6}alkyl$ ,  $O-Si(C_{1-6}alkyl)(C_{1-6}alkyl)(C_{1-6}alkyl)$ ,  $NO_2$ , halo and  $CH_2-S-(CH_2)_n Ar$ ;

$R^4$  is selected from  $C(X)R^5$ ,  $SO_3Ar$ ,  $NH_2$ ,  $NH-C_{1-6}alkyl$ ,  $N(C_{1-6}alkyl)(C_{1-6}alkyl)$ ,  $P(O)(OH)_2$ ,  $P(O)(OC_{1-6}alkyl)_2$ , and  $C(NH_2)=C(CN)_2$ ;

X is selected from O, S, NH and  $N-C_{1-6}alkyl$ ;

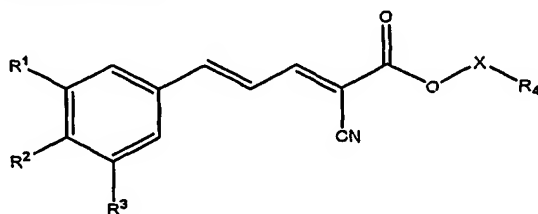
$R^5$  is selected from  $NH_2$ , OH,  $NH(CH_2)_p Ar$ ,  $NH(CH_2)_p OH$ ,  $(CH_2)_p OC_{1-6}alkyl$ ,  $C_{1-6}alkyl$ ,  $C_{1-6}alkoxy$ ,  $NHNH_2$ ,  $NHC(O)NH_2$ ,  $NHC(O)C_{1-6}alkoxy$ , N-morpholino and N-pyrrolidino; and

Ar is an aromatic or heteroaromatic group, unsubstituted or substituted with 1-4 substituents, independently selected from OH,  $C_{1-6}alkyl$ ,  $C_{1-6}alkoxy$ ,  $NH_2$ ,  $NH-C_{1-6}alkyl$ ,  $N(C_{1-6}alkyl)(C_{1-6}alkyl)$ , SH,  $S-C_{1-6}alkyl$ ,  $NO_2$ ,  $CF_3$ ,  $OCF_3$  and halo;

n is 0 to 4; and

p is 1-4.

9. A method of treating a disorder caused or contributed to by vascular endothelial growth factor in an animal in need of such treatment, comprising administering to the animal an effective amount of a compound of Formula IV, or a salt, solvate, prodrug, or hydrate thereof:



IV

wherein

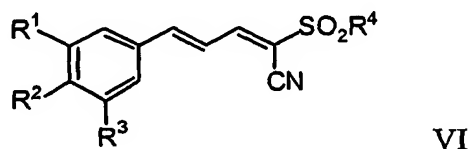
$R^1$ ,  $R^2$  and  $R^3$  are each independently selected from H, OH, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkoxy, NH<sub>2</sub>, NH-C<sub>1-6</sub>alkyl, N(C<sub>1-6</sub>alkyl)(C<sub>1-6</sub>alkyl), SH, S-C<sub>1-6</sub>alkyl, NO<sub>2</sub>, CF<sub>3</sub>, OCF<sub>3</sub> and halo;

$R^4$  is unsubstituted Ar, or Ar substituted with 1-4 substituents, independently selected from C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkoxy and halo;

X is selected from (CH<sub>2</sub>CH<sub>2</sub>O)<sub>n</sub> and (CH<sub>2</sub>)<sub>n</sub>, and

n = 1-4.

10. A method of treating a disorder caused or contributed to by vascular endothelial growth factor in an animal in need of such treatment, comprising administering to the animal an effective amount of a compound of Formula VI, and/or a salt, solvate, prodrug, or hydrate thereof:



wherein

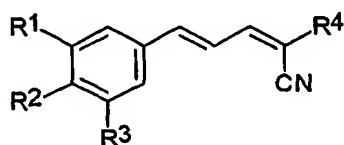
$R^1$ ,  $R^2$  and  $R^3$  are each independently selected from H, OH, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkoxy, NH<sub>2</sub>, NH-C<sub>1-6</sub>alkyl, N(C<sub>1-6</sub>alkyl)(C<sub>1-6</sub>alkyl), SH, S-C<sub>1-6</sub>alkyl, NO<sub>2</sub>, CF<sub>3</sub>, OCF<sub>3</sub> and halo; and

$R^4$  is selected from C<sub>1-6</sub>alkyl, phenyl and pyridyl, wherein phenyl and pyridyl are unsubstituted or substituted with 1-4 substituents, independently selected from C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkoxy and halo.

11. The method of any preceding claim, wherein the animal is a human.
12. The method of claim 8, 9, or 10, wherein expression or levels of vascular endothelial growth factor are upregulated in the disorder.
13. The method of claim 8, 9, or 10, wherein the disorder is cancer, rheumatoid arthritis, retinopathy, atherosclerosis, diabetes, corneal conjunctival vascularization, hemangioma, Kaposi's sarcoma, endometriosis, psoriasis, hemotological

malignancy, lymphoproliferative disorder, myeloproliferative disorder, renal vein occlusion, retinopathy of prematurity, age-related macular degeneration, or bullous disease.

14. The method of claim 13, wherein the disorder is cancer, and the cancer is a solid tumour cancer.
15. The method of claim 14, wherein the solid tumour cancer is breast cancer, pancreatic cancer, colon cancer or brain cancer.
16. The method of claim 11, wherein growth of a tumour is inhibited.
17. Use of a compound for inhibiting secretion of vascular endothelial growth factor in an animal in need of such inhibition, wherein the compound is a compound of Formula I, or a salt, solvate, prodrug, or hydrate thereof:



I

wherein

$R^1$  and  $R^2$  are each independently selected from H, OH,  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy,  $NH_2$ ,  $NH-C_{1-6}$ alkyl,  $N(C_{1-6}alkyl)(C_{1-6}alkyl)$ , SH,  $S-C_{1-6}alkyl$ ,  $O-Si(C_{1-6}alkyl)(C_{1-6}alkyl)(C_{1-6}alkyl)$ ,  $NO_2$ ,  $CF_3$ ,  $OCF_3$  and halo;

$R^3$  is selected from H, OH,  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy,  $NH_2$ ,  $NH-C_{1-6}alkyl$ ,  $N(C_{1-6}alkyl)(C_{1-6}alkyl)$ , SH,  $S-C_{1-6}alkyl$ ,  $O-Si(C_{1-6}alkyl)(C_{1-6}alkyl)(C_{1-6}alkyl)$ ,  $NO_2$ , halo and  $CH_2-S-(CH_2)_n Ar$ ;

$R^4$  is selected from  $C(X)R^5$ ,  $SO_3Ar$ ,  $NH_2$ ,  $NH-C_{1-6}alkyl$ ,  $N(C_{1-6}alkyl)(C_{1-6}alkyl)$ ,  $P(O)(OH)_2$ ,  $P(O)(OC_{1-6}alkyl)_2$ , and  $C(NH_2)=C(CN)_2$ ;

X is selected from O, S, NH and  $N-C_{1-6}alkyl$ ;

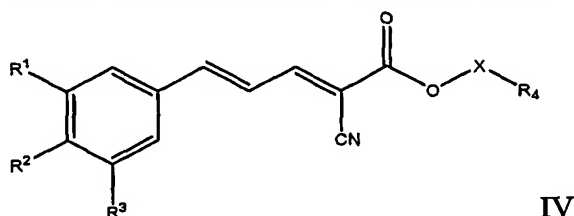
$R^5$  is selected from  $NH_2$ , OH,  $NH(CH_2)_p Ar$ ,  $NH(CH_2)_p OH$ ,  $(CH_2)_p OC_{1-6}alkyl$ ,  $C_{1-6}alkyl$ ,  $C_{1-6}alkoxy$ ,  $NHNH_2$ ,  $NHC(O)NH_2$ ,  $NHC(O)C_{1-6}alkoxy$ , N-morpholino and N-pyrrolidino; and

Ar is an aromatic or heteroaromatic group, unsubstituted or substituted with 1-4 substituents, independently selected from OH, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkoxy, NH<sub>2</sub>, NH-C<sub>1-6</sub>alkyl, N(C<sub>1-6</sub>alkyl)(C<sub>1-6</sub>alkyl), SH, S-C<sub>1-6</sub>alkyl, NO<sub>2</sub>, CF<sub>3</sub>, OCF<sub>3</sub> and halo;

n is 0 to 4; and

p is 1-4.

18. Use of a compound for inhibiting secretion of vascular endothelial growth factor in an animal in need of such inhibition, wherein the compound is a compound of Formula IV, or a salt, solvate, prodrug, or hydrate thereof:



wherein

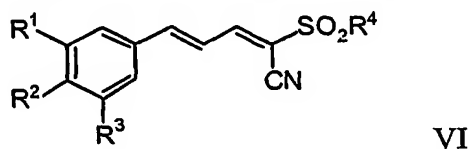
R<sup>1</sup>, R<sup>2</sup> and R<sup>3</sup> are each independently selected from H, OH, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkoxy, NH<sub>2</sub>, NH-C<sub>1-6</sub>alkyl, N(C<sub>1-6</sub>alkyl)(C<sub>1-6</sub>alkyl), SH, S-C<sub>1-6</sub>alkyl, NO<sub>2</sub>, CF<sub>3</sub>, OCF<sub>3</sub> and halo;

R<sup>4</sup> is unsubstituted Ar, or Ar substituted with 1-4 substituents, independently selected from C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkoxy and halo;

X is selected from (CH<sub>2</sub>CH<sub>2</sub>O)<sub>n</sub> and (CH<sub>2</sub>)<sub>n</sub>, and

n = 1-4.

19. Use of a compound for inhibiting secretion of vascular endothelial growth factor in an animal in need of such inhibition, wherein the compound is a compound of Formula VI, and/or a salt, solvate, prodrug, or hydrate thereof:



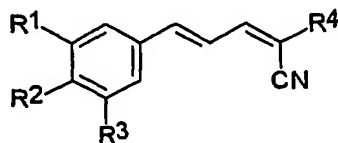
wherein



$R^1$ ,  $R^2$  and  $R^3$  are each independently selected from H, OH,  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy,  $NH_2$ ,  $NH-C_{1-6}$ alkyl,  $N(C_{1-6}alkyl)(C_{1-6}alkyl)$ , SH,  $S-C_{1-6}alkyl$ ,  $NO_2$ ,  $CF_3$ ,  $OCF_3$  and halo; and

$R^4$  is selected from  $C_{1-6}$ alkyl, phenyl and pyridyl, wherein phenyl and pyridyl are unsubstituted or substituted with 1-4 substituents, independently selected from  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy and halo.

20. Use of a compound in the manufacture of a medicament for inhibiting secretion of vascular endothelial growth factor in an animal in need of such inhibition, wherein the compound is a compound of Formula I, or a salt, solvate, prodrug, or hydrate thereof:



wherein

$R^1$  and  $R^2$  are each independently selected from H, OH,  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy,  $NH_2$ ,  $NH-C_{1-6}alkyl$ ,  $N(C_{1-6}alkyl)(C_{1-6}alkyl)$ , SH,  $S-C_{1-6}alkyl$ ,  $O-Si(C_{1-6}alkyl)(C_{1-6}alkyl)(C_{1-6}alkyl)$ ,  $NO_2$ ,  $CF_3$ ,  $OCF_3$  and halo;

$R^3$  is selected from H, OH,  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy,  $NH_2$ ,  $NH-C_{1-6}alkyl$ ,  $N(C_{1-6}alkyl)(C_{1-6}alkyl)$ , SH,  $S-C_{1-6}alkyl$ ,  $O-Si(C_{1-6}alkyl)(C_{1-6}alkyl)(C_{1-6}alkyl)$ ,  $NO_2$ , halo and  $CH_2-S-(CH_2)_n Ar$ ;

$R^4$  is selected from  $C(X)R^5$ ,  $SO_3Ar$ ,  $NH_2$ ,  $NH-C_{1-6}alkyl$ ,  $N(C_{1-6}alkyl)(C_{1-6}alkyl)$ ,  $P(O)(OH)_2$ ,  $P(O)(OC_{1-6}alkyl)_2$ , and  $C(NH_2)=C(CN)_2$ ;

X is selected from O, S, NH and  $N-C_{1-6}alkyl$ ;

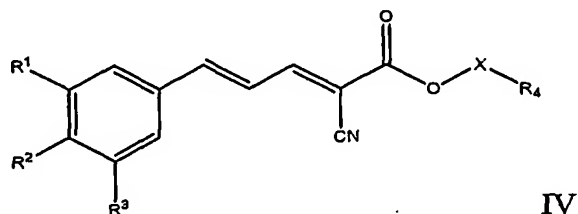
$R^5$  is selected from  $NH_2$ , OH,  $NH(CH_2)_p Ar$ ,  $NH(CH_2)_p OH$ ,  $(CH_2)_p OC_{1-6}alkyl$ ,  $C_{1-6}alkyl$ ,  $C_{1-6}alkoxy$ ,  $NHNH_2$ ,  $NHC(O)NH_2$ ,  $NHC(O)C_{1-6}alkoxy$ , N-morpholino and N-pyrrolidino; and

Ar is an aromatic or heteroaromatic group, unsubstituted or substituted with 1-4 substituents, independently selected from OH,  $C_{1-6}alkyl$ ,  $C_{1-6}alkoxy$ ,  $NH_2$ ,  $NH-C_{1-6}alkyl$ ,  $N(C_{1-6}alkyl)(C_{1-6}alkyl)$ , SH,  $S-C_{1-6}alkyl$ ,  $NO_2$ ,  $CF_3$ ,  $OCF_3$  and halo;

n is 0 to 4; and

p is 1-4.

21. Use of a compound in the manufacture of a medicament for inhibiting secretion of vascular endothelial growth factor in an animal in need of such inhibition, wherein the compound is a compound of Formula IV, or a salt, solvate, prodrug, or hydrate thereof:



wherein

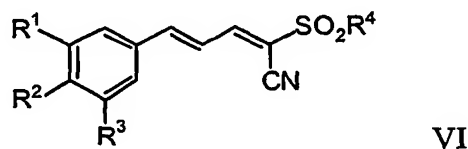
$R^1$ ,  $R^2$  and  $R^3$  are each independently selected from H, OH,  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy,  $NH_2$ ,  $NH-C_{1-6}$ alkyl,  $N(C_{1-6}$ alkyl)( $C_{1-6}$ alkyl), SH,  $S-C_{1-6}$ alkyl,  $NO_2$ ,  $CF_3$ ,  $OCF_3$  and halo;

$R^4$  is unsubstituted Ar, or Ar substituted with 1-4 substituents, independently selected from  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy and halo;

X is selected from  $(CH_2CH_2O)_n$  and  $(CH_2)_n$ , and

$n = 1-4$ .

22. Use of a compound in the manufacture of a medicament for inhibiting secretion of vascular endothelial growth factor in an animal in need of such inhibition, wherein the compound is a compound of Formula VI, and/or a salt, solvate, prodrug, or hydrate thereof:

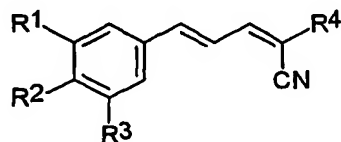


wherein

$R^1$ ,  $R^2$  and  $R^3$  are each independently selected from H, OH,  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy,  $NH_2$ ,  $NH-C_{1-6}$ alkyl,  $N(C_{1-6}$ alkyl)( $C_{1-6}$ alkyl), SH,  $S-C_{1-6}$ alkyl,  $NO_2$ ,  $CF_3$ ,  $OCF_3$  and halo; and

$R^4$  is selected from  $C_{1-6}$ alkyl, phenyl and pyridyl, wherein phenyl and pyridyl are unsubstituted or substituted with 1-4 substituents, independently selected from  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy and halo.

23. Use of a compound for inhibiting effect of vascular endothelial growth factor in an animal in need of such inhibition, wherein the compound is a compound of Formula I, or a salt, solvate, prodrug, or hydrate thereof:



I

wherein

$R^1$  and  $R^2$  are each independently selected from H, OH,  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy,  $NH_2$ ,  $NH-C_{1-6}$ alkyl,  $N(C_{1-6}alkyl)(C_{1-6}alkyl)$ , SH,  $S-C_{1-6}alkyl$ ,  $O-Si(C_{1-6}alkyl)(C_{1-6}alkyl)(C_{1-6}alkyl)$ ,  $NO_2$ ,  $CF_3$ ,  $OCF_3$  and halo;

$R^3$  is selected from H, OH,  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy,  $NH_2$ ,  $NH-C_{1-6}alkyl$ ,  $N(C_{1-6}alkyl)(C_{1-6}alkyl)$ , SH,  $S-C_{1-6}alkyl$ ,  $O-Si(C_{1-6}alkyl)(C_{1-6}alkyl)(C_{1-6}alkyl)$ ,  $NO_2$ , halo and  $CH_2-S-(CH_2)_n Ar$ ;

$R^4$  is selected from  $C(X)R^5$ ,  $SO_3 Ar$ ,  $NH_2$ ,  $NH-C_{1-6}alkyl$ ,  $N(C_{1-6}alkyl)(C_{1-6}alkyl)$ ,  $P(O)(OH)_2$ ,  $P(O)(OC_{1-6}alkyl)_2$ , and  $C(NH_2)=C(CN)_2$ ;

X is selected from O, S, NH and  $N-C_{1-6}alkyl$ ;

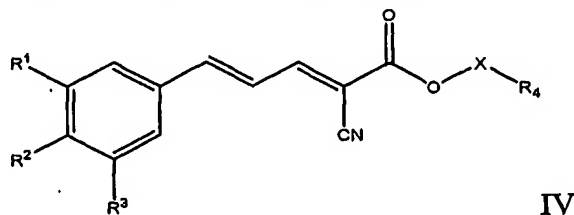
$R^5$  is selected from  $NH_2$ , OH,  $NH(CH_2)_p Ar$ ,  $NH(CH_2)_p OH$ ,  $(CH_2)_p OC_{1-6}alkyl$ ,  $C_{1-6}alkyl$ ,  $C_{1-6}alkoxy$ ,  $NHNH_2$ ,  $NHC(O)NH_2$ ,  $NHC(O)C_{1-6}alkoxy$ , N-morpholino and N-pyrrolidino; and

Ar is an aromatic or heteroaromatic group, unsubstituted or substituted with 1-4 substituents, independently selected from OH,  $C_{1-6}alkyl$ ,  $C_{1-6}alkoxy$ ,  $NH_2$ ,  $NH-C_{1-6}alkyl$ ,  $N(C_{1-6}alkyl)(C_{1-6}alkyl)$ , SH,  $S-C_{1-6}alkyl$ ,  $NO_2$ ,  $CF_3$ ,  $OCF_3$  and halo;

n is 0 to 4; and

p is 1-4.

24. Use of a compound for inhibiting effect of vascular endothelial growth factor in an animal in need of such inhibition, wherein the compound is a compound of Formula IV, or a salt, solvate, prodrug, or hydrate thereof:



wherein

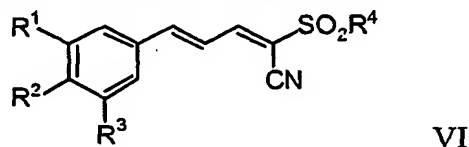
$R^1$ ,  $R^2$  and  $R^3$  are each independently selected from H, OH,  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy,  $NH_2$ ,  $NH-C_{1-6}$ alkyl,  $N(C_{1-6}$ alkyl)( $C_{1-6}$ alkyl), SH,  $S-C_{1-6}$ alkyl,  $NO_2$ ,  $CF_3$ ,  $OCF_3$  and halo;

$R^4$  is unsubstituted Ar, or Ar substituted with 1-4 substituents, independently selected from  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy and halo;

X is selected from  $(CH_2CH_2O)_n$  and  $(CH_2)_n$ , and

$n = 1-4$ .

25. Use of a compound for inhibiting effect of vascular endothelial growth factor in an animal in need of such inhibition, wherein the compound is a compound of Formula VI, and/or a salt, solvate, prodrug, or hydrate thereof:

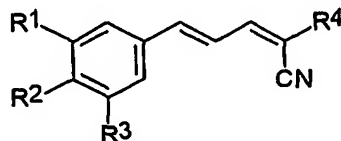


wherein

$R^1$ ,  $R^2$  and  $R^3$  are each independently selected from H, OH,  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy,  $NH_2$ ,  $NH-C_{1-6}$ alkyl,  $N(C_{1-6}$ alkyl)( $C_{1-6}$ alkyl), SH,  $S-C_{1-6}$ alkyl,  $NO_2$ ,  $CF_3$ ,  $OCF_3$  and halo; and

$R^4$  is selected from  $C_{1-6}$ alkyl, phenyl and pyridyl, wherein phenyl and pyridyl are unsubstituted or substituted with 1-4 substituents, independently selected from  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy and halo.

26. Use of a compound in the manufacture of a medicament for inhibiting effect of vascular endothelial growth factor in an animal in need of such inhibition, wherein the compound is a compound of Formula I, or a salt, solvate, prodrug, or hydrate thereof:



I

wherein

$R^1$  and  $R^2$  are each independently selected from H, OH,  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy,  $NH_2$ ,  $NH-C_{1-6}$ alkyl,  $N(C_{1-6}alkyl)(C_{1-6}alkyl)$ , SH,  $S-C_{1-6}alkyl$ ,  $O-Si(C_{1-6}alkyl)(C_{1-6}alkyl)(C_{1-6}alkyl)$ ,  $NO_2$ ,  $CF_3$ ,  $OCF_3$  and halo;

$R^3$  is selected from H, OH,  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy,  $NH_2$ ,  $NH-C_{1-6}alkyl$ ,  $N(C_{1-6}alkyl)(C_{1-6}alkyl)$ , SH,  $S-C_{1-6}alkyl$ ,  $O-Si(C_{1-6}alkyl)(C_{1-6}alkyl)(C_{1-6}alkyl)$ ,  $NO_2$ , halo and  $CH_2-S-(CH_2)_n Ar$ ;

$R^4$  is selected from  $C(X)R^5$ ,  $SO_3Ar$ ,  $NH_2$ ,  $NH-C_{1-6}alkyl$ ,  $N(C_{1-6}alkyl)(C_{1-6}alkyl)$ ,  $P(O)(OH)_2$ ,  $P(O)(OC_{1-6}alkyl)_2$ , and  $C(NH_2)=C(CN)_2$ ;

X is selected from O, S, NH and  $N-C_{1-6}alkyl$ ;

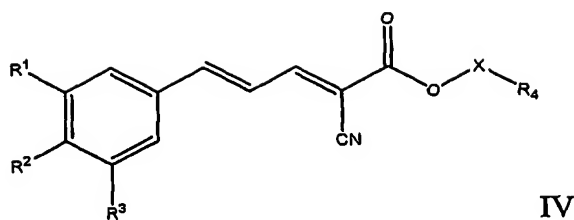
$R^5$  is selected from  $NH_2$ , OH,  $NH(CH_2)_p Ar$ ,  $NH(CH_2)_p OH$ ,  $(CH_2)_p OC_{1-6}alkyl$ ,  $C_{1-6}alkyl$ ,  $C_{1-6}alkoxy$ ,  $NHNH_2$ ,  $NHC(O)NH_2$ ,  $NHC(O)C_{1-6}alkoxy$ , N-morpholino and N-pyrrolidino; and

Ar is an aromatic or heteroaromatic group, unsubstituted or substituted with 1-4 substituents, independently selected from OH,  $C_{1-6}alkyl$ ,  $C_{1-6}alkoxy$ ,  $NH_2$ ,  $NH-C_{1-6}alkyl$ ,  $N(C_{1-6}alkyl)(C_{1-6}alkyl)$ , SH,  $S-C_{1-6}alkyl$ ,  $NO_2$ ,  $CF_3$ ,  $OCF_3$  and halo;

n is 0 to 4; and

p is 1-4.

27. Use of a compound in the manufacture of a medicament for inhibiting effect of vascular endothelial growth factor in an animal in need of such inhibition, wherein the compound is a compound of Formula IV, or a salt, solvate, prodrug, or hydrate thereof:



wherein

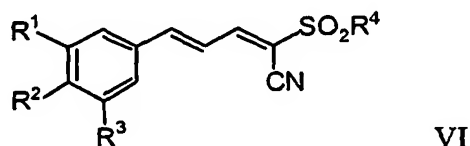
$R^1$ ,  $R^2$  and  $R^3$  are each independently selected from H, OH,  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy,  $NH_2$ ,  $NH-C_{1-6}$ alkyl,  $N(C_{1-6}$ alkyl)( $C_{1-6}$ alkyl), SH,  $S-C_{1-6}$ alkyl,  $NO_2$ ,  $CF_3$ ,  $OCF_3$  and halo;

$R^4$  is unsubstituted Ar, or Ar substituted with 1-4 substituents, independently selected from  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy and halo;

X is selected from  $(CH_2CH_2O)_n$  and  $(CH_2)_n$ , and

$n = 1-4$ .

28. Use of a compound in the manufacture of a medicament for inhibiting effect of vascular endothelial growth factor in an animal in need of such inhibition, wherein the compound is a compound of Formula VI, and/or a salt, solvate, prodrug, or hydrate thereof:



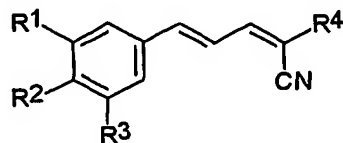
wherein

$R^1$ ,  $R^2$  and  $R^3$  are each independently selected from H, OH,  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy,  $NH_2$ ,  $NH-C_{1-6}$ alkyl,  $N(C_{1-6}$ alkyl)( $C_{1-6}$ alkyl), SH,  $S-C_{1-6}$ alkyl,  $NO_2$ ,  $CF_3$ ,  $OCF_3$  and halo; and

$R^4$  is selected from  $C_{1-6}$ alkyl, phenyl and pyridyl, wherein phenyl and pyridyl are unsubstituted or substituted with 1-4 substituents, independently selected from  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy and halo.

29. The use of any one of claims 23-28, wherein the effect of vascular endothelial growth factor is angiogenesis, vasculogenesis, arteriogenesis, vascular permeability, or inflammation.

30. Use of a compound for treating a disorder related to vascular endothelial growth factor in an animal in need of such treatment, wherein the compound is a compound of Formula I, or a salt, solvate, prodrug, or hydrate thereof:



I

wherein

$R^1$  and  $R^2$  are each independently selected from H, OH,  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy,  $NH_2$ ,  $NH-C_{1-6}$ alkyl,  $N(C_{1-6}alkyl)(C_{1-6}alkyl)$ , SH,  $S-C_{1-6}alkyl$ ,  $O-Si(C_{1-6}alkyl)(C_{1-6}alkyl)(C_{1-6}alkyl)$ ,  $NO_2$ ,  $CF_3$ ,  $OCF_3$  and halo;

$R^3$  is selected from H, OH,  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy,  $NH_2$ ,  $NH-C_{1-6}alkyl$ ,  $N(C_{1-6}alkyl)(C_{1-6}alkyl)$ , SH,  $S-C_{1-6}alkyl$ ,  $O-Si(C_{1-6}alkyl)(C_{1-6}alkyl)(C_{1-6}alkyl)$ ,  $NO_2$ , halo and  $CH_2-S-(CH_2)_n Ar$ ;

$R^4$  is selected from  $C(X)R^5$ ,  $SO_3 Ar$ ,  $NH_2$ ,  $NH-C_{1-6}alkyl$ ,  $N(C_{1-6}alkyl)(C_{1-6}alkyl)$ ,  $P(O)(OH)_2$ ,  $P(O)(OC_{1-6}alkyl)_2$ , and  $C(NH_2)=C(CN)_2$ ;

X is selected from O, S, NH and  $N-C_{1-6}alkyl$ ;

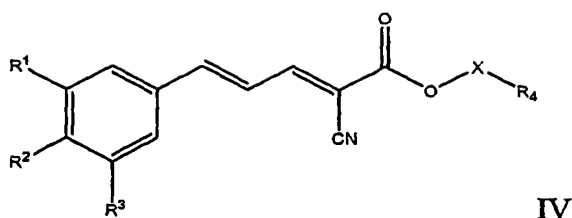
$R^5$  is selected from  $NH_2$ , OH,  $NH(CH_2)_p Ar$ ,  $NH(CH_2)_p OH$ ,  $(CH_2)_p OC_{1-6}alkyl$ ,  $C_{1-6}alkyl$ ,  $C_{1-6}alkoxy$ ,  $NHNH_2$ ,  $NHC(O)NH_2$ ,  $NHC(O)C_{1-6}alkoxy$ , N-morpholino and N-pyrrolidino; and

Ar is an aromatic or heteroaromatic group, unsubstituted or substituted with 1-4 substituents, independently selected from OH,  $C_{1-6}alkyl$ ,  $C_{1-6}alkoxy$ ,  $NH_2$ ,  $NH-C_{1-6}alkyl$ ,  $N(C_{1-6}alkyl)(C_{1-6}alkyl)$ , SH,  $S-C_{1-6}alkyl$ ,  $NO_2$ ,  $CF_3$ ,  $OCF_3$  and halo;

n is 0 to 4; and

p is 1-4.

31. Use of a compound for treating a disorder related to vascular endothelial growth factor in an animal in need of such treatment, wherein the compound is a compound of Formula IV, or a salt, solvate, prodrug, or hydrate thereof:



wherein

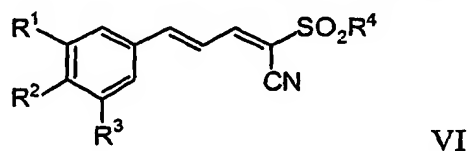
$R^1$ ,  $R^2$  and  $R^3$  are each independently selected from H, OH,  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy,  $NH_2$ ,  $NH-C_{1-6}$ alkyl,  $N(C_{1-6}$ alkyl)( $C_{1-6}$ alkyl), SH,  $S-C_{1-6}$ alkyl,  $NO_2$ ,  $CF_3$ ,  $OCF_3$  and halo;

$R^4$  is unsubstituted Ar, or Ar substituted with 1-4 substituents, independently selected from  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy and halo;

X is selected from  $(CH_2CH_2O)_n$  and  $(CH_2)_n$ , and

$n = 1-4$ .

32. Use of a compound for treating a disorder related to vascular endothelial growth factor in an animal in need of such treatment, wherein the compound is a compound of Formula VI, and/or a salt, solvate, prodrug, or hydrate thereof:



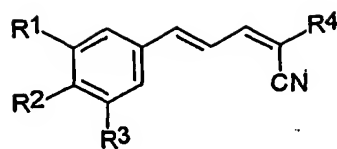
wherein

$R^1$ ,  $R^2$  and  $R^3$  are each independently selected from H, OH,  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy,  $NH_2$ ,  $NH-C_{1-6}$ alkyl,  $N(C_{1-6}$ alkyl)( $C_{1-6}$ alkyl), SH,  $S-C_{1-6}$ alkyl,  $NO_2$ ,  $CF_3$ ,  $OCF_3$  and halo; and

$R^4$  is selected from  $C_{1-6}$ alkyl, phenyl and pyridyl, wherein phenyl and pyridyl are unsubstituted or substituted with 1-4 substituents, independently selected from  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy and halo.

33. Use of a compound in the manufacture of a medicament for treating a disorder related to vascular endothelial growth factor in an animal in need of such treatment, wherein the compound is a compound of Formula I, or a salt, solvate, prodrug, or hydrate thereof:





I

wherein

$R^1$  and  $R^2$  are each independently selected from H, OH,  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy,  $NH_2$ ,  $NH-C_{1-6}$ alkyl,  $N(C_{1-6}alkyl)(C_{1-6}alkyl)$ , SH,  $S-C_{1-6}alkyl$ ,  $O-Si(C_{1-6}alkyl)(C_{1-6}alkyl)(C_{1-6}alkyl)$ ,  $NO_2$ ,  $CF_3$ ,  $OCF_3$  and halo;

$R^3$  is selected from H, OH,  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy,  $NH_2$ ,  $NH-C_{1-6}alkyl$ ,  $N(C_{1-6}alkyl)(C_{1-6}alkyl)$ , SH,  $S-C_{1-6}alkyl$ ,  $O-Si(C_{1-6}alkyl)(C_{1-6}alkyl)(C_{1-6}alkyl)$ ,  $NO_2$ , halo and  $CH_2-S-(CH_2)_n Ar$ ;

$R^4$  is selected from  $C(X)R^5$ ,  $SO_3Ar$ ,  $NH_2$ ,  $NH-C_{1-6}alkyl$ ,  $N(C_{1-6}alkyl)(C_{1-6}alkyl)$ ,  $P(O)(OH)_2$ ,  $P(O)(OC_{1-6}alkyl)_2$ , and  $C(NH_2)=C(CN)_2$ ;

X is selected from O, S, NH and  $N-C_{1-6}alkyl$ ;

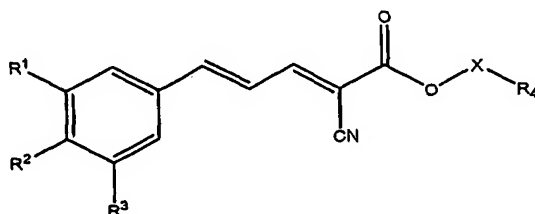
$R^5$  is selected from  $NH_2$ , OH,  $NH(CH_2)_p Ar$ ,  $NH(CH_2)_p OH$ ,  $(CH_2)_p OC_{1-6}alkyl$ ,  $C_{1-6}alkyl$ ,  $C_{1-6}alkoxy$ ,  $NHNH_2$ ,  $NHC(O)NH_2$ ,  $NHC(O)C_{1-6}alkoxy$ , N-morpholino and N-pyrrolidino; and

Ar is an aromatic or heteroaromatic group, unsubstituted or substituted with 1-4 substituents, independently selected from OH,  $C_{1-6}alkyl$ ,  $C_{1-6}alkoxy$ ,  $NH_2$ ,  $NH-C_{1-6}alkyl$ ,  $N(C_{1-6}alkyl)(C_{1-6}alkyl)$ , SH,  $S-C_{1-6}alkyl$ ,  $NO_2$ ,  $CF_3$ ,  $OCF_3$  and halo;

n is 0 to 4; and

p is 1-4.

34. Use of a compound in the manufacture of a medicament for treating a disorder related to vascular endothelial growth factor in an animal in need of such treatment, wherein the compound is a compound of Formula IV, or a salt, solvate, prodrug, or hydrate thereof:



IV

wherein

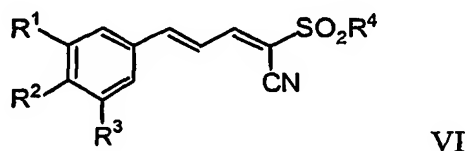
$R^1$ ,  $R^2$  and  $R^3$  are each independently selected from H, OH,  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy,  $NH_2$ ,  $NH-C_{1-6}$ alkyl,  $N(C_{1-6}$ alkyl)( $C_{1-6}$ alkyl), SH,  $S-C_{1-6}$ alkyl,  $NO_2$ ,  $CF_3$ ,  $OCF_3$  and halo;

$R^4$  is unsubstituted Ar, or Ar substituted with 1-4 substituents, independently selected from  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy and halo;

X is selected from  $(CH_2CH_2O)_n$  and  $(CH_2)_n$ , and

$n = 1-4$ .

35. Use of a compound in the manufacture of a medicament for treating a disorder related to vascular endothelial growth factor in an animal in need of such treatment, wherein the compound is a compound of Formula VI, and/or a salt, solvate, prodrug, or hydrate thereof:



wherein

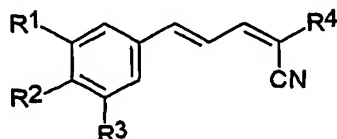
$R^1$ ,  $R^2$  and  $R^3$  are each independently selected from H, OH,  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy,  $NH_2$ ,  $NH-C_{1-6}$ alkyl,  $N(C_{1-6}$ alkyl)( $C_{1-6}$ alkyl), SH,  $S-C_{1-6}$ alkyl,  $NO_2$ ,  $CF_3$ ,  $OCF_3$  and halo; and

$R^4$  is selected from  $C_{1-6}$ alkyl, phenyl and pyridyl, wherein phenyl and pyridyl are unsubstituted or substituted with 1-4 substituents, independently selected from  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy and halo.

36. The use of claim 33, 34, or 35, wherein expression or levels of vascular endothelial growth factor are upregulated in the disorder.
37. The use of claim 33, 34, or 35, wherein the disorder is cancer, rheumatoid arthritis, retinopathy, atherosclerosis, diabetes, corneal conjunctival vascularization, hemangioma, Kaposi's sarcoma, endometriosis, psoriasis, hemotological malignancy, lymphoproliferative disorder, myeloproliferative disorder, renal vein

occlusion, retinopathy of prematurity, age-related macular degeneration, or bullous disease.

38. The use of claim 37, wherein the disorder is cancer and the cancer is solid tumour cancer.
39. The use of claim 38, wherein the solid tumour cancer is breast cancer, pancreatic cancer, colon cancer, or brain cancer.
40. The use of claim 38, wherein growth of a tumour is inhibited.
41. A packaged pharmaceutical comprising a compound and a label or instructions for use of the compound for inhibiting secretion of vascular endothelial growth factor, inhibiting effect of vascular endothelial growth factor, or treating a disorder related to vascular endothelial growth factor in an animal in need of such inhibition, wherein the compound is a compound of Formula I, or a salt, solvate, prodrug, or hydrate thereof:



I

wherein

$R^1$  and  $R^2$  are each independently selected from H, OH,  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy,  $NH_2$ ,  $NH-C_{1-6}$ alkyl,  $N(C_{1-6}alkyl)(C_{1-6}alkyl)$ , SH,  $S-C_{1-6}alkyl$ ,  $O-Si(C_{1-6}alkyl)(C_{1-6}alkyl)(C_{1-6}alkyl)$ ,  $NO_2$ ,  $CF_3$ ,  $OCF_3$  and halo;

$R^3$  is selected from H, OH,  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy,  $NH_2$ ,  $NH-C_{1-6}alkyl$ ,  $N(C_{1-6}alkyl)(C_{1-6}alkyl)$ , SH,  $S-C_{1-6}alkyl$ ,  $O-Si(C_{1-6}alkyl)(C_{1-6}alkyl)(C_{1-6}alkyl)$ ,  $NO_2$ , halo and  $CH_2-S-(CH_2)_n$  Ar;

$R^4$  is selected from  $C(X)R^5$ ,  $SO_3Ar$ ,  $NH_2$ ,  $NH-C_{1-6}alkyl$ ,  $N(C_{1-6}alkyl)(C_{1-6}alkyl)$ ,  $P(O)(OH)_2$ ,  $P(O)(OC_{1-6}alkyl)_2$ , and  $C(NH_2)=C(CN)_2$ ;

X is selected from O, S, NH and  $N-C_{1-6}alkyl$ ;

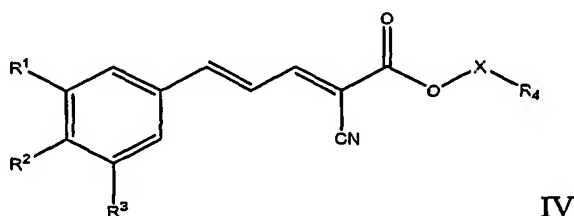
$R^5$  is selected from  $NH_2$ ,  $OH$ ,  $NH(CH_2)_pAr$ ,  $NH(CH_2)_pOH$ ,  $(CH_2)_pOC_{1-6}alkyl$ ,  $C_{1-6}alkyl$ ,  $C_{1-6}alkoxy$ ,  $NHNH_2$ ,  $NHC(O)NH_2$ ,  $NHC(O)C_{1-6}alkoxy$ ,  $N$ -morpholino and  $N$ -pyrrolidino; and

$Ar$  is an aromatic or heteroaromatic group, unsubstituted or substituted with 1-4 substituents, independently selected from  $OH$ ,  $C_{1-6}alkyl$ ,  $C_{1-6}alkoxy$ ,  $NH_2$ ,  $NH-C_{1-6}alkyl$ ,  $N(C_{1-6}alkyl)(C_{1-6}alkyl)$ ,  $SH$ ,  $S-C_{1-6}alkyl$ ,  $NO_2$ ,  $CF_3$ ,  $OCF_3$  and halo;

$n$  is 0 to 4; and

$p$  is 1-4.

42. A packaged pharmaceutical comprising a compound and a label or instructions for use of the compound for inhibiting secretion of vascular endothelial growth factor, inhibiting effect of vascular endothelial growth factor, or treating a disorder related to vascular endothelial growth factor in an animal in need of such inhibition, wherein the compound is a compound of Formula IV, or a salt, solvate, prodrug, or hydrate thereof:



wherein

$R^1$ ,  $R^2$  and  $R^3$  are each independently selected from  $H$ ,  $OH$ ,  $C_{1-6}alkyl$ ,  $C_{1-6}alkoxy$ ,  $NH_2$ ,  $NH-C_{1-6}alkyl$ ,  $N(C_{1-6}alkyl)(C_{1-6}alkyl)$ ,  $SH$ ,  $S-C_{1-6}alkyl$ ,  $NO_2$ ,  $CF_3$ ,  $OCF_3$  and halo;

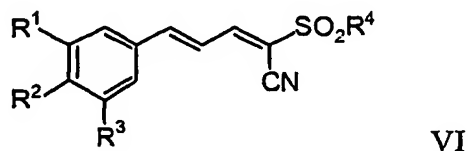
$R^4$  is unsubstituted  $Ar$ , or  $Ar$  substituted with 1-4 substituents, independently selected from  $C_{1-6}alkyl$ ,  $C_{1-6}alkoxy$  and halo;

$X$  is selected from  $(CH_2CH_2O)_n$  and  $(CH_2)_n$ , and

$n = 1-4$ .

43. A packaged pharmaceutical comprising a compound and a label or instructions for use of the compound for inhibiting secretion of vascular endothelial growth factor, inhibiting effect of vascular endothelial growth factor, or treating a disorder related

to vascular endothelial growth factor in an animal in need of such inhibition, wherein the compound is a compound of Formula VI, and/or a salt, solvate, prodrug, or hydrate thereof:

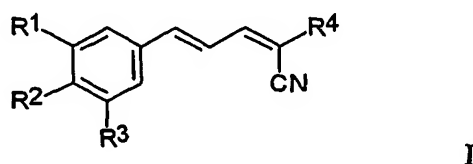


wherein

$R^1$ ,  $R^2$  and  $R^3$  are each independently selected from H, OH,  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy,  $NH_2$ ,  $NH-C_{1-6}$ alkyl,  $N(C_{1-6}$ alkyl)( $C_{1-6}$ alkyl), SH,  $S-C_{1-6}$ alkyl,  $NO_2$ ,  $CF_3$ ,  $OCF_3$  and halo; and

$R^4$  is selected from  $C_{1-6}$ alkyl, phenyl and pyridyl, wherein phenyl and pyridyl are unsubstituted or substituted with 1-4 substituents, independently selected from  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy and halo.

44. The use of claim 41, wherein the compound inhibits migration and/or proliferation of vascular endothelial cells.
45. The use of claim 44, wherein the compound inhibits vascular restenosis.
46. The use of claim 44, wherein the compound is provided as part of a drug-eluting stent.
47. A medical device comprising:
  - (a) a substrate having a surface; and
  - (b) a coating disposed on the surface, said coating comprising a polymer matrix including a compound of Formula I, or a salt, solvate, prodrug, or hydrate thereof:



wherein

$R^1$  and  $R^2$  are each independently selected from H, OH,  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy,  $NH_2$ ,  $NH-C_{1-6}$ alkyl,  $N(C_{1-6}alkyl)(C_{1-6}alkyl)$ , SH,  $S-C_{1-6}alkyl$ ,  $O-Si(C_{1-6}alkyl)(C_{1-6}alkyl)(C_{1-6}alkyl)$ ,  $NO_2$ ,  $CF_3$ ,  $OCF_3$  and halo;

$R^3$  is selected from H, OH,  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy,  $NH_2$ ,  $NH-C_{1-6}alkyl$ ,  $N(C_{1-6}alkyl)(C_{1-6}alkyl)$ , SH,  $S-C_{1-6}alkyl$ ,  $O-Si(C_{1-6}alkyl)(C_{1-6}alkyl)(C_{1-6}alkyl)$ ,  $NO_2$ , halo and  $CH_2-S-(CH_2)_n Ar$ ;

$R^4$  is selected from  $C(X)R^5$ ,  $SO_3Ar$ ,  $NH_2$ ,  $NH-C_{1-6}alkyl$ ,  $N(C_{1-6}alkyl)(C_{1-6}alkyl)$ ,  $P(O)(OH)_2$ ,  $P(O)(OC_{1-6}alkyl)_2$ , and  $C(NH_2)=C(CN)_2$ ;

X is selected from O, S, NH and  $N-C_{1-6}alkyl$ ;

$R^5$  is selected from  $NH_2$ , OH,  $NH(CH_2)_p Ar$ ,  $NH(CH_2)_p OH$ ,  $(CH_2)_p OC_{1-6}alkyl$ ,  $C_{1-6}alkyl$ ,  $C_{1-6}alkoxy$ ,  $NHNH_2$ ,  $NHC(O)NH_2$ ,  $NHC(O)C_{1-6}alkoxy$ , N-morpholino and N-pyrrolidino; and

Ar is an aromatic or heteroaromatic group, unsubstituted or substituted with 1-4 substituents, independently selected from OH,  $C_{1-6}alkyl$ ,  $C_{1-6}alkoxy$ ,  $NH_2$ ,  $NH-C_{1-6}alkyl$ ,  $N(C_{1-6}alkyl)(C_{1-6}alkyl)$ , SH,  $S-C_{1-6}alkyl$ ,  $NO_2$ ,  $CF_3$ ,  $OCF_3$  and halo;

n is 0 to 4; and p is 1-4.

48. The device of claim 47, wherein the polymer is non bioerodible.
49. The device of claim 47, wherein the polymer is bioerodible.
50. The device of claim 47, wherein the substrate is selected from catheters, implantable vascular access ports, blood storage bags, blood tubing, central venous catheters, arterial catheters, vascular grafts, intraaortic balloon pumps, heart valves, cardiovascular sutures, artificial hearts, a pacemaker, ventricular assist pumps, extracorporeal devices, blood filters, hemodialysis units, hemoperfusion units, plasmapheresis units, filters adapted for deployment in a blood vessel, intraocular lenses, shunts for hydrocephalus, dialysis grafts, colostomy bag attachment devices, ear drainage tubes, leads for pace makers and implantable defibrillators, and osteointegrated orthopedic devices.
51. The device of claim 50, which is a vascular stent.

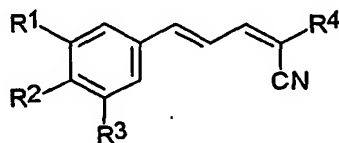
52. A method for treating a mammalian organism to obtain a desired local or systemic physiological or pharmacological effect, comprising: administering a pharmaceutically effective amount of a drug by placing in said mammal the device of any of claims 47-50 to a mammal.
53. The method of claim 1, wherein said animal has, or is at risk for developing, arteriovenous malformations (AVM), meningioma, vascular restenosis, angiofibroma, dermatitis, endometriosis, hemophilic joints, hypertrophic scars, inflammatory disease, pyogenic granuloma, scleroderma, synovitis, trachoma or vascular adhesions.
54. The method of claim 1, wherein said animal has, or is at risk for developing, abnormal proliferation of fibrovascular tissue, acne rosacea, acquired immune deficiency syndrome, artery occlusion, atopic keratitis, bacterial ulcers, Bechets disease, blood borne tumors, carotid obstructive disease, chemical burns, choroidal neovascularization, chronic inflammation, chronic retinal detachment, chronic uveitis, chronic vitritis, contact lens overwear, corneal graft rejection, corneal neovascularization, corneal graft neovascularization, Crohn's disease, Bales disease, epidemic keratoconjunctivitis, fungal ulcers, Herpes simplex infections, Herpes zoster infections, hyperviscosity syndromes, Kaposi's sarcoma, leukemia, lipid degeneration, Lyme's disease, marginal keratolysis, Mooren ulcer, Mycobacteria infections other than leprosy, myopia, ocular neovascular disease, optic pits, Osler-Weber syndrome (Osler-Weber-Rendu), osteoarthritis, Pagets disease, pars planitis, pemphigoid, phylectenulosis, polyarteritis, post-laser complications, protozoan infections, pseudoxanthoma elasticum, pterygium keratitis sicca, radial keratotomy, retinal neovascularization, retinopathy of prematurity, retrolental fibroplasias, sarcoid, scleritis, sickle cell anemia, Sogrens syndrome, solid tumors, Stargarts disease, Steven's Johnson disease, superior limbic keratitis, syphilis, systemic lupus, Terrien's marginal degeneration, toxoplasmosis, trauma, tumors of Ewing sarcoma, tumors of neuroblastoma, tumors of osteosarcoma, tumors of retinoblastoma, tumors of rhabdomyosarcoma, ulcerative colitis, vein occlusion, Vitamin A deficiency or

Wegeners sarcoidosis.

55. The method of claim 1, wherein said animal has, or is at risk for developing, diabetes; parasitic disease; abnormal wound healing; hypertrophy following surgery, burns, injury or trauma; inhibition of hair growth; inhibition of ovulation and corpus luteum formation; inhibition of implantation or inhibition of embryo development in the uterus.
56. The method of claim 1, wherein said animal has, or is at risk for developing, graft rejection, lung inflammation, nephrotic syndrome, preeclampsia, edema associated with brain tumors, ascites associated with malignancies, Meigs' syndrome, pericardial effusion, pericarditis or pleural effusion.
57. The method of claim 1, wherein said animal has, or is at risk for developing, a vascularized solid tumor, a metastatic tumor or metastases from a primary tumor.
58. The method of claim 57, further comprising administering to said animal a therapeutically effective amount of at least a second anti-cancer agent.
59. The method of claim 58, wherein said at least a second anti-cancer agent is a chemotherapeutic agent, radiotherapeutic agent, anti-angiogenic agent, apoptosis-inducing agent or anti-tubulin drug or a tumor-targeted chemotherapeutic agent, radiotherapeutic agent, anti-angiogenic agent, apoptosis-inducing agent or anti-tubulin drug.
60. The method of claim 59, wherein said at least a second anti-cancer agent is an anti tubulin drug selected from the group consisting of colchicine, taxol, vinblastine, vincristine, vindesine and a combretastatin or a tumor-targeted anti-tubulin drug selected from the group consisting of colchicine, taxol, vinblastine, vincristine, vindesine and a combretastatin.
61. The method of claim 1, for treating endometriosis.



62. The method of claim 61, wherein the compound is administered by an intra-uterine or intra-peritoneal route.
63. The method of claim 1, for treating an ocular neovascular disease in a patient.
64. The method of claim 63, wherein said neovascular disease is selected from the group consisting of ischemic retinopathy, intraocular neovascularization, age-related macular degeneration, corneal neovascularization, retinal neovascularization, choroidal neovascularization, diabetic macular edema, diabetic retina ischemia, diabetic retinal edema, and proliferative diabetic retinopathy.
65. A drug eluting device dimensioned for implantation in the vitreous of a human eye, which device includes an amount of a compound which is released from the device over a sustained period of time to treat an ocular neovascular disease in a patient, said compound represented in Formula I, or a salt, solvate, prodrug, or hydrate thereof:



I

wherein

$R^1$  and  $R^2$  are each independently selected from H, OH,  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy,  $NH_2$ ,  $NH-C_{1-6}$ alkyl,  $N(C_{1-6}alkyl)(C_{1-6}alkyl)$ , SH,  $S-C_{1-6}alkyl$ ,  $O-Si(C_{1-6}alkyl)(C_{1-6}alkyl)(C_{1-6}alkyl)$ ,  $NO_2$ ,  $CF_3$ ,  $OCF_3$  and halo;

$R^3$  is selected from H, OH,  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy,  $NH_2$ ,  $NH-C_{1-6}alkyl$ ,  $N(C_{1-6}alkyl)(C_{1-6}alkyl)$ , SH,  $S-C_{1-6}alkyl$ ,  $O-Si(C_{1-6}alkyl)(C_{1-6}alkyl)(C_{1-6}alkyl)$ ,  $NO_2$ , halo and  $CH_2-S-(CH_2)_n Ar$ ;

$R^4$  is selected from  $C(X)R^5$ ,  $SO_3 Ar$ ,  $NH_2$ ,  $NH-C_{1-6}alkyl$ ,  $N(C_{1-6}alkyl)(C_{1-6}alkyl)$ ,  $P(O)(OH)_2$ ,  $P(O)(OC_{1-6}alkyl)_2$ , and  $C(NH_2)=C(CN)_2$ ;

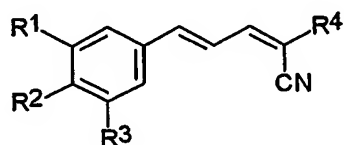
X is selected from O, S, NH and  $N-C_{1-6}alkyl$ ;

$R^5$  is selected from  $NH_2$ ,  $OH$ ,  $NH(CH_2)_pAr$ ,  $NH(CH_2)_pOH$ ,  $(CH_2)_pOC_{1-6}alkyl$ ,  $C_{1-6}alkyl$ ,  $C_{1-6}alkoxy$ ,  $NHNH_2$ ,  $NHC(O)NH_2$ ,  $NHC(O)C_{1-6}alkoxy$ ,  $N$ -morpholino and  $N$ -pyrrolidino; and

$Ar$  is an aromatic or heteroaromatic group, unsubstituted or substituted with 1-4 substituents, independently selected from  $OH$ ,  $C_{1-6}alkyl$ ,  $C_{1-6}alkoxy$ ,  $NH_2$ ,  $NH$ - $C_{1-6}alkyl$ ,  $N(C_{1-6}alkyl)(C_{1-6}alkyl)$ ,  $SH$ ,  $S$ - $C_{1-6}alkyl$ ,  $NO_2$ ,  $CF_3$ ,  $OCF_3$  and halo;

$n$  is 0 to 4; and  $p$  is 1-4.

66. The method of claim 1, for treating atherosclerosis in a patient.
67. The method of claim 1, for treating an inflammatory disease in a patient.
68. The method of claim 67, wherein the inflammatory disease is arthritis.
69. A method of interfering with angiogenesis, neovascularization or lymphangiogenesis in a mammal having a condition characterized by angiogenesis, neovascularization or lymphangiogenesis, comprising administering to said mammal an effective amount of a compound represented in Formula I, or a salt, solvate, prodrug, or hydrate thereof:



wherein

$R^1$  and  $R^2$  are each independently selected from  $H$ ,  $OH$ ,  $C_{1-6}alkyl$ ,  $C_{1-6}alkoxy$ ,  $NH_2$ ,  $NH$ - $C_{1-6}alkyl$ ,  $N(C_{1-6}alkyl)(C_{1-6}alkyl)$ ,  $SH$ ,  $S$ - $C_{1-6}alkyl$ ,  $O$ - $Si(C_{1-6}alkyl)(C_{1-6}alkyl)(C_{1-6}alkyl)$ ,  $NO_2$ ,  $CF_3$ ,  $OCF_3$  and halo;

$R^3$  is selected from  $H$ ,  $OH$ ,  $C_{1-6}alkyl$ ,  $C_{1-6}alkoxy$ ,  $NH_2$ ,  $NH$ - $C_{1-6}alkyl$ ,  $N(C_{1-6}alkyl)(C_{1-6}alkyl)$ ,  $SH$ ,  $S$ - $C_{1-6}alkyl$ ,  $O$ - $Si(C_{1-6}alkyl)(C_{1-6}alkyl)(C_{1-6}alkyl)$ ,  $NO_2$ , halo and  $CH_2$ - $S$ -( $CH_2$ ) $_n$   $Ar$ ;

$R^4$  is selected from  $C(X)R^5$ ,  $SO_3Ar$ ,  $NH_2$ ,  $NH$ - $C_{1-6}alkyl$ ,  $N(C_{1-6}alkyl)(C_{1-6}alkyl)$ ,  $P(O)(OH)_2$ ,  $P(O)(OC_{1-6}alkyl)_2$ , and  $C(NH_2)=C(CN)_2$ ;

X is selected from O,S, NH and N-C<sub>1-6</sub>alkyl;

R<sup>5</sup> is selected from NH<sub>2</sub>, OH, NH(CH<sub>2</sub>)<sub>p</sub>Ar, NH(CH<sub>2</sub>)<sub>p</sub>OH, (CH<sub>2</sub>)<sub>p</sub>OC<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkoxy, NHNH<sub>2</sub>, NHC(O)NH<sub>2</sub>, NHC(O)C<sub>1-6</sub>alkoxy, N-morpholino and N-pyrrolidino; and

Ar is an aromatic or heteroaromatic group, unsubstituted or substituted with 1-4 substituents, independently selected from OH, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkoxy, NH<sub>2</sub>, NH-C<sub>1-6</sub>alkyl, N(C<sub>1-6</sub>alkyl)(C<sub>1-6</sub>alkyl), SH, S-C<sub>1-6</sub>alkyl, NO<sub>2</sub>, CF<sub>3</sub>, OCF<sub>3</sub> and halo;

n is 0 to 4; and p is 1-4.